Effects of pulmonary rehabilitation on exacerbation number and severity in people with COPD: An historical cohort study using electronic health records

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Abbreviations:
COPD = chronic obstructive pulmonary disease, PR = pulmonary rehabilitation, AECOPD = acute exacerbations of COPD, GP = general practice, CPRD = Clinical Practice Research Datalink, HES = Hospital Episode Statistics, ICD = International Classification of Disease, CI = confidence intervals, IQR = interquartile range, LOS = length of stay, RCT = randomised controlled trial, FEV_1 = forced expiratory volume in 1 second, QOL = quality of life, QALY = Quality-Adjusted Life Year, IRB = Institutional Review Board.

Conflict of Interest Disclosures

JKQ reports grants from the Medical Research Council (MRC), GlaxoSmithKline (GSK), British Lung Foundation (BLF), Wellcome Trust, during the conduct of the study, and personal fees from AstraZeneca and Boehringer Ingelheim, outside of the submitted work. MS reports other current research grants from Arthritis Research UK, Public Health England and the EU EITHealth Programme, with no conflicts of interest. SS reports grants from the National Institute for Health Research (NIHR), GlaxoSmithKline (GSK), Boehringer Ingelheim and Novartis and personal fees from Novartis and AstraZeneca. All other authors report no other conflicts of interest.

Abstract

Background: In previous systematic reviews, predominantly of randomised controlled trials, pulmonary rehabilitation (PR) has been shown to reduce hospital admissions for acute exacerbations of COPD (AECOPD). However, findings have been less consistent for cohort studies. We aimed to compare rates of hospitalized and general practice (GP) treated AECOPD before and after PR.

Methods: Using anonymised data from the Clinical Practice Research Datalink and Hospital Episode Statistics, hospital admissions and GP visits for AECOPD were compared one year before and after PR in patients referred for PR. Exacerbation rates were also compared between individuals eligible and referred for PR with those eligible and not referred.

Results: 69,089 (64%) of the COPD patients in the cohort were eligible for PR. Of these, only 6,436 (9.3%) were recorded as having been referred for rehabilitation. 62, 019 (89.8%) were not referred and 634 (0.98%) declined referral. When combining GP and hospital exacerbations, people who were eligible and were referred for PR had a slightly higher but not statistically significant exacerbation rate (2.83 exacerbations/patient-year 95% CI: 2.66, 3.00) than those who were eligible but not referred (2.17 exacerbations/patient-year 95% CI: 2.11, 2.24).

Conclusions: This study found that less than 10% of patients who were eligible for PR were actually referred. Patients who were eligible and referred for (but not necessarily completed) PR did not have fewer GP visits and hospitalizations for AECOPD in the year after PR compared to those not referred or compared to the year before PR.

Introduction

AECOPD contribute to disease progression and mortality, and are important for patients and health care providers; negatively impacting on health related quality of life,[1,2] leading to a decline in pulmonary function[3] and increased use of health care.[4] Patients experience on average 1-3 treated exacerbations per year[5] with up to 10% of patients dying during a hospital admission for AECOPD[6] and up to 25% within a year of admission for AECOPD.[7]

Pulmonary rehabilitation is a key component of the multi-disciplinary management of COPD[8] and can improve exercise capacity, dyspnoea, activities of daily living, muscle strength, self-efficacy, and quality of life.[9] Given the evidence of these benefits, a recent Cochrane Editorial stated that no further systematic reviews are required to show that pulmonary rehabilitation improves patient-related outcomes.[10]

A recent update in a 2016 systematic review by Puhan *et al*[11] found that pulmonary rehabilitation reduced hospital readmissions but results were heterogenous and evidence did not show a statistically significant effect of rehabilitation on mortality. Results from randomised controlled trials (RCTs) in another recent review suggested that PR reduces subsequent readmissions but pooled results from cohort studies and before-and-after studies did not [12]. Therefore the evidence for the benefits of PR on reducing hospital admissions remains unclear. Furthermore, no study has investigated the effect of pulmonary rehabilitation on reducing hospital admissions or milder GP treated events, particularly in less severe COPD patients; arguably the ones who make up the majority of referrals for pulmonary rehabilitation. This is important as GP managed exacerbations have been associated with declines in exercise capacity and muscle strength, and reduced physical activity can impact on quality of life.[13]

This study aimed to compare the rates of hospitalized and general practice (GP) treated AECOPD before and after PR, using primary care data from the UK Clinical Practice Research Datalink (CPRD), linked with Hospital Episode Statistics (HES). Firstly, exacerbation rates were compared in those who were eligible and referred for PR versus those who were eligible and were not referred during all time observed (Observation 1: Figure 1). Secondly, we compared exacerbation rates before and after PR in those who were eligible for PR and were referred over the whole study period (Observation 2). Thirdly we compared one year before and one year after PR in those who were eligible and were referred (Observation 3). Fourthly, we compared exacerbation rates one year before and one year after PR for those who actually completed the course of rehabilitation (Observation 4). Finally, we examined

length of stay for those who were hospitalized for AECOPD at least once in the year before and the year after rehabilitation.

Materials & Methods

Study Subjects

People over the age of 35 who had a GP recorded diagnosis of COPD using a validated definition[14] and did not have alpha one antitrypsin deficiency but had at least one year of historical data before the study start were included. People were deemed eligible for pulmonary rehabilitation if they had a pulmonary rehabilitation code which suggested they were eligible (see Appendix for code list), or if they had an MRC score of 3 or more, or if they had 2 or more GP treated AECOPD in a year or one hospital admission for an AECOPD in a year. This definition was based on current clinical practice for referral[15]. We used a previously validated definition to identify AECOPD in CPRD and HES.[16,17] IRB approval was not required as this study used anonymous patient data. Approval was obtained from the CPRD Independent Scientific Advisory Committee (ISAC), prior to study start which oversees research involving CPRD data (protocol ref: 15_193R; available on request).

Study design

This is a propensity weighted cohort study and also a before-after analysis was carried out. The STROBE (strengthening the reporting of observational studies in epidemiology) guidelines[18] were used in this study.

Methods

CPRD is an electronic database of UK general practice data that has been widely used for research.[19] It contains anonymised records for over 13 million patients, of whom 4.4 million are currently registered with a practice that is contributing data to CPRD, representing about 9% of the UK population. Data held include information on consultations, diagnoses, tests, referrals to secondary care and prescriptions from primary care as well as some lifestyle data. Data are predominantly recorded using a system of “Read codes”; a hierarchical system of codes which include diagnoses, clinical signs, symptoms and lifestyle characteristics. Around 60% of the patients included in the CPRD have been linked to HES, an administrative database containing information on all episodes of National Health Service (NHS) inpatient care in England[16]. Diagnoses in HES are recorded using International Classification of Disease version 10 (ICD-10) codes (see Appendix).

Figure 1 shows the study design and the four main observation spells. The date of entry to the cohort was the latest of the 1st January 2004, diagnosis of COPD and date of being eligible for (or having done) pulmonary rehabilitation. The end of the follow up was the earliest of the end of the study period (31st March 2014), the last date of data collection, the date of death or the date of transfer to another practice. Controls (COPD patients not referred for rehabilitation) were age, gender and CPRD practice matched to COPD patients who were referred for pulmonary rehabilitation. The date of referral for rehabilitation was the index date for the match. Patients were deemed eligible for PR if they had a MRC score of 3 or higher, had 2 or more GP exacerbations in a 1 year time period or had 1 hospital admission for an AECOPD in 1 year. Patients were considered ineligible if they had cerebrovascular disease, rheumatoid arthritis, depression, heart failure, or stroke.

Analysis

Baseline characteristics were tabulated and Chi-square tests performed to test the association between the pulmonary rehabilitation status and categorical explanatory variables. Exacerbation rates of AECOPD were compared in the year before and one year after pulmonary rehabilitation, only on patients who were ever referred for rehabilitation. Recorded visits to the GP for an exacerbation and hospital visits were analysed separately and then in combination for patients who were recorded as having pulmonary rehabilitation and compared with patients who were eligible, but were not referred for pulmonary rehabilitation. Length of hospital stay was also analysed in people who were eligible and referred for pulmonary rehabilitation in the year before and year after pulmonary rehabilitation using the Wilcoxon signed-rank test. Statistical calculations used Version 14 of the Stata statistical package.[20]

The observation period for each patient was defined as an interval of time at risk between 2 successive dates (beginning on the first event date and ending on the day before the last event date). An event date could be an imputed patient birthday (1 July on any year from the patient birth year), date of patient entry to observation by CPRD, date of patient exit from observation by CPRD, date of initiation of pulmonary rehabilitation, date 1 year before initiation, date 1 year after initiation, or date of diagnosis of one of the following diseases: COPD, asthma, cerebrovascular disease, rheumatoid arthritis, depression, heart failure, or stroke. The outcomes were numbers of AECOPD reported by the patient's GP (determined in CPRD), numbers of COPD exacerbations leading to hospitalizations (determined in HES and excluding elective admissions), and total numbers of both, in the duration of observation for that patient. We used Poisson generalized linear models, with exposure time at risk

expressed in person-years, and Huber variances clustered by practice. Analyses were done on 4 subsets of observation periods and are listed in the **Appendix**.

Propensity weights were calculated using a propensity score from a logistic regression model, with Huber variances clustered by practice, with pulmonary rehabilitation treatment as the outcome, and confounding covariates as the predictors. Methods for the propensity scoring and list of confounders are described in the **Appendix**.

Results

Figure 2. Flow Chart of Eligibility for the Study

Figure 2 shows the flow of subjects included and Table 1 describes the baseline demographics and co-morbidities of patients included in the analysis. 108,041 patients were included; of these 53% were male. A total of 38,952 (36%) COPD patients were not eligible for pulmonary rehabilitation; i.e. did not meet our eligibility criteria. Of the 69,089 eligible; 6,436 (9.3%) were recorded a having been referred to or completed pulmonary rehabilitation, 62,019 (89.8%) were not referred and 634 (0.9%) were referred but declined. The mean age (standard deviation) of patients who received rehabilitation was 64.53 (10.17). Table 2 provides the baseline respiratory related characteristics of the COPD patients. The average follow up time for all eligible patients was 3.29 years, and for those eligible and referred for PR 4.57 years.

Exacerbation rates in COPD patients referred for pulmonary rehabilitation versus those not referred (Observation 1)

Figure 3 and Table 3 show a) the exacerbation rate per person-year at risk and the 95% confidence intervals (CIs) comparing individuals who were not referred with individuals who were referred for PR; and b) the exacerbation rate ratios (95% CI) in unweighted and propensity weighted analyses comparing people not referred with people referred. If patients received an extra diagnosis after the initial time point from when pulmonary rehabilitation started they were given extra weighting in the analysis. The total results (GP and hospital exacerbations) showed that people who were referred for pulmonary rehabilitation had a slightly higher but not significant exacerbation rate of 2.83 exacerbations/person-year (95% CI 2.66, 3.00) than individuals who were not referred (2.17 95% CI 2.11, 2.24)

Exacerbation rates in COPD patients before and after pulmonary rehabilitation (Observation 2)

Figure 4 and Table 4 show a) the exacerbation rate per person-year at risk and the 95% CIs before and after pulmonary rehabilitation and b) the exacerbation rate ratios (95% CI) in unweighted and propensity weighted analyses comparing people before and after rehabilitation. The total results (GP and hospital exacerbations) showed that after pulmonary rehabilitation, people had a slightly higher but not statistically significant exacerbation rate of 3.15 exacerbations/person-year (95% CI: 2.97, 3.33) compared to before PR (2.79 95% CI: 2.65, 2.93). Higher exacerbation rate ratios were observed for hospital AECOPD than for AECOPD seen in primary care. Table 4 provides the detailed results.

Exacerbation rates: one year before and one year after pulmonary rehabilitation in COPD patients who were referred (Observation 3)

AECOPD rates per person-year at risk (95% CI) 1 year before and 1 year after initiation of pulmonary rehabilitation are shown in Figure 5 (a). The same trend was observed in the before-after comparison in each analysis as observed in Figure 4. Higher exacerbation rates per person-year at risk were observed for individuals in the year following referral for pulmonary rehabilitation (3.18 95% CI 3.02, 3.35) compared to the year prior to pulmonary rehabilitation (3.04 95% CI 2.88, 3.20). Figure 5 (b) shows the exacerbation rate ratio (95% CI) in unweighted and propensity weighted analyses comparing 1 year before and 1 year after pulmonary rehabilitation. Higher exacerbation rate ratios were observed in primary care compared to hospital events. Table 5 provides the detailed scores for exacerbation rates per person-year at risk observed in the before-after analysis.

Exacerbation rates one year before and one year after pulmonary rehabilitation in those who completed pulmonary rehabilitation (Observation 4)

Figure 6 (a) shows the exacerbation rate per person-year at risk (95% CI) 1 year before and 1 year after pulmonary rehabilitation in individuals who completed rehabilitation (see Table 6 for scores). And Figure 6 (b) shows the exacerbation rate ratio (95% CI) in unweighted and propensity weighted analyses comparing people completing pulmonary rehabilitation 1 year before and 1 year after. . The propensity weighted scores revealed that patients who completed pulmonary rehabilitation had a higher exacerbation rate per person-year at risk (3.49 95% CI 3.09, 3.95) in the year after compared to the year before pulmonary rehabilitation (3.31 95% CI 2.89, 3.79). Finally, higher exacerbation rate ratios were observed in hospital exacerbations compared to GP exacerbations.

Length of hospital stay

When looking at length of hospital stay (LOS) in a subset of 305 patients who were hospitalized for AECOPD at least once in the year before and once in the year after rehabilitation, there was no reduction in the median length of stay following pulmonary rehabilitation. Figure 7 shows that the median LOS one year before rehabilitation was 4 days (IQR = 2-8 days) compared to one year after in which the median LOS was 7 days (IQR = 3-18).

Discussion

Less than 10% of patients with COPD in the UK who were eligible for pulmonary rehabilitation in this study were actually referred. Patients who were eligible and referred for pulmonary rehabilitation from primary care did not have fewer GP visits or hospital admissions for AECOPD one year after rehabilitation when compared to those who were eligible but were not referred. The same trend was observed when comparing exacerbation rates in one year before and one year after rehabilitation in those eligible and referred and limiting the analysis to a subset of patients who had evidence of having completed pulmonary rehabilitation. This is in agreement with more recent studies that have shown no benefit of rehabilitation on hospital readmissions[11]. When comparing GP exacerbations with hospital exacerbations, COPD exacerbation severity did not appear to reduce in the year after pulmonary rehabilitation. Furthermore we found no reduction in hospital LOS for exacerbations of COPD pre- and post- pulmonary rehabilitation.

One of the key strengths of this study is the large cohort of COPD patients examined over a long period of time with exacerbation data from both primary and secondary care. Additionally, the data used are from routinely collected primary care and hospital sources, reflecting real life patients seen in every day clinical practice. This was a large cohort study and the results are similar to those of other studies including a retrospective cohort study in California by Nguyen et al.,[21] which compared rates of exacerbations in 558 patients who received pulmonary rehabilitation in the stable state to 1,114 patients who did not. 12 months after the programme, 10% of the non-intervention group were hospitalized for an exacerbation, whereas 18% of the pulmonary rehabilitation group were hospitalized.

However, there are several weaknesses that might explain the differences between these findings and those of systematic reviews and some RCTs. Firstly, records from CPRD and HES may not be a complete and accurate reflection of what COPD patients are actually experiencing as not all patients receiving

pulmonary rehabilitation will be recorded by clinicians and captured in electronic health records. Indeed in this study less than 10% of COPD patients who were eligible were referred. Secondly, we have not analysed the compliance with rehabilitation but only investigated patients who were captured as having been referred for pulmonary rehabilitation. As only around 40% of people referred for pulmonary rehabilitation complete a course,[22] the lack of benefit seen here is likely to be underestimated. Another weakness of our study and using electronic health data is that we were not able to examine the nature of PR programmes that patients were referred to such as the number of sessions, intensity and content of the rehabilitation to compare them with UK standards and guidelines. We are aware that patients may have been referred to PR via other sources and thus not captured as having been referred in this dataset but given the nature of health care provision in the UK with the GP at the centre, this is likely to be minimal. Certainly of those referred, a higher proportion are likely to have completed than has been recorded, and improved coding of completion of pulmonary rehabilitation (for which Read codes do exist) would aid commissioners and pulmonary rehabilitation providers in determining the effects and benefits of pulmonary rehabilitation.

One of the reasons why results from our study differed from those of RCTs is that patients in the RCTs completed the course of pulmonary rehabilitation and may have had greater compliance, and thus effectiveness of pulmonary rehabilitation on reducing admission may be greater. Another issue is that pulmonary rehabilitation programmes vary significantly, and although guidelines for pulmonary rehabilitation programmes exist,[15] differing interpretations of these guidelines can occur in routine practice, thus programmes may vary between centres across the country.[22] As previously mentioned we were not able to assess the content and quality of the PR programmes.

Another important consideration is how education within rehabilitation programmes is delivered to and received by patients. One study which randomised patients into a comprehensive care management plan (CCMP) versus usual care found that mortality was higher in the CCMP group.[23] This group received COPD education on self-management and an action plan for identification and treatment of their exacerbations. The higher mortality figure suggests that despite having education about self-management, some patients still do not seek advice and treatment early enough to reduce exacerbations, or conversely that they become more vigilant and aware of their symptoms. Finally, the severity of COPD patients who are eligible for pulmonary rehabilitation is different, and this too may contribute to the lack of exacerbation reduction. However, when we restricted the

analysis to hospital events only, we still did not see a reduction in exacerbations. There may be unobserved confounding despite propensity matching. Reductions in LOS after rehabilitation have also been reported in some RCTs[24,25] and observational studies[26] whereas a reduction in LOS was not observed in this cohort. Reasons for this may include the fact that patients in our analysis are older and frailer and possibly have more comorbidities than those who participated in the RCTs. Furthermore we only considered hospitalizations for AECOPD and did not include other causes of hospitalizations.

There are a number of potential biases that might affect recorded exacerbation rates between the various comparator groups in our study, particularly confounding by indication (i.e. those presenting with exacerbations are more likely to be referred) and the impact of attendance on health behaviours where the provision of education during PR might actually increase because of a heighted awareness of treatment need. In addition, variations in exacerbation frequency over time, may have had an impact on the year to year comparison in those referred for PR.

Our study and several other observational studies have not replicated the findings from RCTs and our recent systematic review[12] which have suggested that pulmonary rehabilitation is effective at reducing the frequency of exacerbations, however a reductionn AECOPD has been observed in RCTs of pulmonary rehabilitation post exacerbation. RCT programmes may have more effective content, delivery, follow up and motivation than standard rehabilitation courses. Surveys have suggested that the provision of pulmonary rehabilitation services can vary both within and between countries.[27] This highlights the need for pulmonary rehabilitation courses to be accredited and able to demonstrate adherence to the standards found in RCTs to be of maximum benefit to patients. This study also highlights the need for GPs to record completers of pulmonary rehabilitation for measurement of more accurate and meaningful outcomes.

Pulmonary rehabilitation has many other benefits aside from reducing healthcare consumption and exacerbations. Although there is no convincing biological rationale to suggest that PR will reduce the frequency of lung events, there is evidence that early pulmonary rehabilitation following an exacerbation can lead to a reduced number of days spent in hospital[25]. Numerous studies have also shown pulmonary rehabilitation improves health-related quality of life (QOL), activity limitation, perceived breathlessness, and exercise capacity[28,29]. These improvements may be arguably more important to patients who suffer from COPD than reducing healthcare consumption and thus pulmonary rehabilitation remains an important intervention to patients.

Despite this, pulmonary rehabilitation is still underutilised.[30,31] Major challenges in realising the effectiveness of pulmonary rehabilitation are that a proportion of people who have COPD and hence AECOPD have not been diagnosed,[32] and a large proportion of those who have been diagnosed and are eligible for pulmonary rehabilitation are not being referred[22]. In addition the England and Wales national COPD audit programme, which includes data from both the acute hospital settings and primary care, reported that 31% of patients referred for rehabilitation did not attend the initial assessment, and 40% of those referred did not complete the programme[22,33]. A small proportion of individuals are offered pulmonary rehabilitation following an AECOPD but even fewer will take up a course[34]. While we are likely to have overestimated the number of eligible but not referred people in this dataset, as we cannot account for the main reasons people may not be eligible, our findings are in keeping with the UK pulmonary rehabilitation audit data[22]. Further research is needed to look at reasons why patients with COPD who are eligible for pulmonary rehabilitation are not being referred, reasons why those who are being referred are not completing programmes, and the effect on readmissions. Previous studies have suggested that current smoking, a lack of perceived benefit and depression are all likely to represent barriers to uptake or increase non-completion.[35]

Conclusions

Using data from primary care and hospital records, this study found that patients who were referred for pulmonary rehabilitation did not have fewer GP and hospital AECOPD one year following pulmonary rehabilitation when compared to those who were not referred. Any effect of PR on exacerbation frequency was not detectable through routinely recorded primary care data. Findings from our study, along with results from other studies and audit data, have highlighted a major clinical issue in that large proportions of patients are either not starting or are not completing pulmonary rehabilitation. As an intervention it has great potential to be effective if patients are referred and can adhere to properly-designed and -delivered programmes. Future research looking at the effects of pulmonary rehabilitation on GP and hospital visits for COPD should take into account the important issues relating to the referral of patients and adherence to programmes, and the national COPD audit should monitor the content of rehabilitation more closely.

Acknowledgements

The Chartered Society of Physiotherapy (CSP) funded a research project on COPD with Imperial College London. The CSP were not involved in the design or conduct of this study. However, we wish to acknowledge helpful comments received from an Expert Group coordinated by CSP which

included Alison Coe, Anne Bruton, Becca Bryant, Brenda O'Neill, Ian Culligan, Jamie Forrester, Jane Mullins, Judith Colligan, Julia Bott, Kat Savage, Marianne Milligan, Marie Buxton, Noel Baxter, Rhiannon Kendrick and Sally Singh. Imperial College London is grateful for support from the NW London NIHR Collaboration for Leadership in Applied Health Research & Care (CLAHRC), the Imperial NIHR Biomedical Research Centre, and the Imperial Centre for Patient Safety and Service Quality (CPSSQ). Sally Singh is supported by the EM CLAHRC. All other researchers involved were independent of funders.

Author Contributions

EM and TP produced the first draft and edited subsequent revisions. KR, RN and MJ, carried out the statistical analyses and commented on revisions. JKQ, MS and SS conceived the study and reviewed subsequent drafts. JKQ is identified as the guarantor of the paper.

Transparency Declaration

EM affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Responsibility for Data

As Principal Investigator Dr Jennifer Quint had full access to all the data in the study and she takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects.

Figure 3. a) Exacerbation rate per person-year at risk (95% CI) comparing individuals who were eligible for pulmonary rehabilitation and not referred with individuals who were eligible and referred during the study period; b) exacerbation rate ratio (95% CI) in unweighted and propensity weighted analyses comparing people eligible and not referred for pulmonary rehabilitation with people eligible and referred for pulmonary rehabilitation during the study period.

Figure 4 a) Exacerbation rate per person-year at risk (95% CI) in the year following pulmonary rehabilitation in individuals who were eligible for pulmonary rehabilitation and referred; b)

exacerbation rate ratio (95% CI) in unweighted and propensity weighted analyses comparing people eligible and referred for pulmonary rehabilitation before and after pulmonary rehabilitation .

Figure 5 a) Exacerbation rate per person-year at risk (95% CI) 1 year before and 1 year after pulmonary rehabilitation in individuals who were eligible for pulmonary rehabilitation and referred; b) exacerbation rate ratio (95% CI) in unweighted and propensity weighted analyses comparing people eligible and referred for pulmonary rehabilitation 1 year before and 1 year after pulmonary rehabilitation.

Figure 6 a) Exacerbation rate per person-year at risk (95% CI) 1 year before and 1 year after pulmonary rehabilitation in individuals who were eligible for pulmonary rehabilitation and completed b) exacerbation rate ratio (95% CI) in unweighted and propensity weighted analyses comparing people completing pulmonary rehabilitation 1 year before and 1 year after pulmonary rehabilitation.

Figure 7 Median length of stay in hospital (number of days) one year before and one year after pulmonary rehabilitation only in individuals who completed pulmonary rehabilitation.

Table 1: Baseline characteristics of COPD patients: demographic and general medical

Characteristic	Category	Pulmonary Rehabilitation Status				
		Not Eligible (38,953)	Eligible			Eligible (all categories) (69,089)
			Referred for PR (6,436)	Not referred for PR (62,019)	Declined PR (634)	
Gender	Male	22,044 (56.59)	3,569 (55.45)	31,340 (50.53)	378 (59.62)	35,287(51.07)
	Female	16,909 (43.41)	2,867 (44.55)	30,679 (49.47)	256 (40.38)	33,802(48.93)
Cerebrovascular Disease	Absent	18,760 (48.16)	2,624 (40.77)	25,089 (40.45)	278 (43.85)	27,991(40.51)
	Present	20,193 (51.84)	3,812 (59.23)	36,930 (59.55)	356 (56.15)	41,098(59.49)
Rheumatoid Arthritis	Absent	37,979 (97.50)	6,225 (96.72)	59,905 (96.59)	617 (97.32)	66,747(96.61)
	Present	974 (2.50)	211 (3.28)	2,114 (3.41)	17 (2.68)	2,342(3.39)
Depression	Absent	27,368 (70.26)	3,930 (61.06)	39,162 (63.15)	455 (71.77)	43,547(63.03)
	Present	11,585 (29.74)	2,506 (38.94)	22,857 (36.85)	179 (28.23)	25,542(36.97)
Heart Failure	Absent	33,312 (85.52)	5,609 (87.15)	51,066 (82.34)	587 (92.59)	57,262(82.88)
	Present	5,641 (14.48)	827 (12.85)	10,953 (17.66)	47 (7.41)	11,827(17.12)
Stroke	Absent	34,267 (87.97)	5,727 (88.98)	53,608 (86.44)	585 (92.27)	59,920(86.73)
	Present	4,686 (12.03)	709 (11.02)	8,411 (13.56)	49 (7.73)	9,169(13.27)
Age	N/A	67.14 (11.93)	64.53 (10.17)	67.68 (11.32)	64.91 (10.26)	67.36(11.25)

Notes:
1. The table is based on the data of 108,041 patients in all.
2. In the columns, figures are as follows. For age: mean (SD). For other variables: number (% of population).

Table 2: Baseline characteristics of COPD patients: respiratory-related

Characteristic	Category	Pulmonary Rehabilitation Status				
		Not Eligible (38,953)	Eligible			Eligible (all categories) (69,089)
			Referred for PR (6,436)	Not referred for PR (62,019)	Declined PR (634)	
Smoking status	Non-smoker	1,468 (3.77)	119 (1.85)	1,897 (3.06)	17 (2.68)	2,033(2.94)
	Current smoker	19,149 (49.16)	3,090 (48.01)	30,105 (48.54)	293 (46.21)	33,488(48.47)
	Ex-smoker	17,442 (44.78)	3,206 (49.81)	29,440 (47.47)	323 (50.95)	32,969(47.72)
	Missing	*894 (2.30)*	*21 (0.33)*	*577 (0.93)*	*1 (0.16)*	*599(0.87)*
Spirometry Severity Grade	1 (less severe)	6,362 (16.33)	587 (9.12)	8,156 (13.15)	117 (18.45)	8,860(12.82)
	2	12,401 (31.84)	2,658 (41.30)	23,430 (37.78)	336 (53.00)	26,424(38.25)
	3	4,599 (11.81)	2,159 (33.55)	13,761 (22.19)	120 (18.93)	16,040(23.22)
	4 (more severe)	1,079 (2.77)	750 (11.65)	3,863 (6.23)	13 (2.05)	4,626(6.70)
	Missing	*14,512 (37.26)*	*282 (4.38)*	*12,809 (20.65)*	*48 (7.57)*	*13,139(19.02)*
Record for asthma	Absent	23,213 (59.59)	2,659 (41.31)	30,343 (48.93)	352 (55.52)	33,354(48.28)
	Present	15,740 (40.41)	3,777 (58.69)	31,676 (51.07)	282 (44.48)	35,735(51.72)
MRC Score	1 (less severe)	9,818(25.20)	1,436(22.31)	11,184(18.03)	356(56.15)	12,976(18.78)
	2	7,011(18.00)	2,589(40.23)	18,070(29.14)	273(43.06)	20,932(30.30)
	3	0(0.00)	1,521(23.63)	10,543(17.00)	0(0.00)	12,064(17.46)
	4	0(0.00)	585(9.09)	4,977(8.02)	0(0.00)	5,562(8.05)
	5 (more severe)	0(0.00)	92(1.43)	1,292(2.08)	0(0.00)	1,384(2.00)
	Missing	22,124(56.80)	213(3.31)	15,953(25.72)	5(0.79)	16,171(23.41)

Notes:
1. The table is based on the data of 108,041 patients in all.
2. In the columns, figures for variables are number (% of population)

Table 3 Exacerbation rates per person-year at risk (unweighted and propensity weighted): Comparison of individuals who were eligible but not referred for PR with individuals who were eligible and referred for PR during the study period.

			Unweighted	***Propensity weighted***
Exacerbation type	*Person-years*	*Events*	*Rate (95% CI)*	*Rate (95% CI)*
GP event count:				
Not referred for PR	181478.38	349557	1.926 (1.864, 1.990)	1.931 (1.869, 1.995)
Referred for PR	16613.67	42365	2.550 (2.388, 2.723)	2.538 (2.379, 2.708)
HES event count:				
Not referred for PR	181478.38	43380	0.239 (0.231, 0.247)	0.240 (0.232, 0.249)
Referred for PR	16613.67	4864	0.293 (0.269, 0.319)	0.287 (0.265, 0.312)
Total event count (GP + HES):				
Not referred for PR	181478.38	392937	2.165 (2.101, 2.231)	2.171 (2.106, 2.238)
Referred for PR	16613.67	47229	2.843 (2.671, 3.026)	2.825 (2.657,3.004)

Table 4. Exacerbation rates per person-year at risk (unweighted and propensity weighted): Comparison of individuals who were eligible and referred for PR before and after rehabilitation.

			Unweighted	***Propensity weighted***
Exacerbation type	*Person-years*	*Events*	*Rate (95% CI)*	*Rate (95% CI)*
GP event count:				
Before PR	9798.52	24473	2.498 (2.379, 2.622)	2.521 (2.400, 2.647)
After PR	9397.96	26610	2.831 (2.658, 3.016)	2.816 (2.648, 2.996)
HES event count:				
Before PR	9798.52	2598	0.265 (0.239, 0.294)	0.270 (0.243, 0.299)
After PR	9397.96	3224	0.343 (0.317, 0.371)	0.328 (0.303, 0.355)
Total event count (GP + HES):				
Before PR	9798.52	27071	2.763 (2.630, 2.902)	2.790 (2.654, 2.933)
After PR	9397.96	29834	3.175 (2.991, 3.369)	3.145 (2.967, 3.333)

Table 5. Exacerbation rates per person-year at risk (unweighted and propensity weighted): Comparison of individuals who were eligible and referred for PR in the year before and the year after PR.

			Unweighted	***Propensity weighted***
Exacerbation type	*Person-years*	*Events*	*Rate (95% CI)*	*Rate (95% CI)*
GP				
Year before PR	3515.73	9674	2.752 (2.614, 2.897)	2.757 (2.618, 2.904)
Year after PR	3602.33	10454	2.902 (2.757, 3.055)	2.894 (2.750, 3.046)
HES:				
Year before PR	3515.73	977	0.278 (0.246, 0.315)	0.280 (0.248, 0.317)
Year after PR	3602.33	1040	0.289 (0.258, 0.323)	0.284 (0.254, 0.318)
Total (GP + HES):				
Year before PR	3515.73	10651	3.030 (2.874, 3.193)	3.038 (2.881, 3.203)
Year after PR	3602.33	11494	3.191 (3.031, 3.359)	3.178 (3.019, 3.345)

Table 6. Exacerbation rates per person-year at risk (unweighted and propensity weighted): Comparison of individuals who were eligible and completed PR 1 year before and 1 year after PR.

			Unweighted	***Propensity weighted***

Exacerbation type	*Person-years*	*Events*	*Rate (95% CI)*	*Rate (95% CI)*
GP:				
Year before PR	269.68	796	2.952 (2.605, 3.345)	2.951 (2.595, 3.356)
Year after PR	258.10	801	3.103 (2.758, 3.493)	3.096 (2.750, 3.484)
HES:				
Year before PR	269.68	94	0.349 (0.246, 0.495)	0.360 (0.254, 0.510)
Year after PR	258.10	106	0.411 (0.290, 0.581)	0.398 (0.284, 0.556)
Total (GP + HES):				
Year before PR	269.68	890	3.300 (2.888, 3.771)	3.311 (2.890, 3.794)
Year after PR	258.10	907	3.514 (3.107, 3.974)	3.493 (3.091, 3.948)

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